

REMARKS

The Claim Amendments

Claims 70-75 constitute the pending claims in the present application. Claims 73 and 74 are withdrawn.

Rejection of Claims 70-72 and 75 Under 35 U.S.C. § 112, 1st Paragraph

The Examiner has rejected claims 70-72 and 75 under 35 U.S.C. § 112, 1st paragraph, for allegedly failing to comply with the enablement requirement. Specifically, the Examiner argues that the application allegedly lacks a working example and that the claimed method allegedly would not be effective in treating all types of cancer. Applicants respectfully traverse.

A. In Vivo Working Example

The Examiner, citing MPEP § 2164.02, acknowledges that Applicants need not have actually reduced the invention to practice prior to filing the application, and also acknowledges that the lack of a working example is “only one factor to be considered” when assessing enablement. However, despite the Examiner’s acknowledgement that the pending application need not have an *in vivo* working example to satisfy the enablement requirement, the Examiner continues to base his enablement rejection, in part, on the ground that the specification does not provide any *in vivo* working examples in support of the claimed method.

MPEP § 2164.02, the section of the MPEP cited by the Examiner in raising the enablement rejection, states that “[T]he mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it.” This section of the MPEP also states “[T]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.” The pending application, in view of the skilled worker’s understanding of cancer and the development of cancer therapies, provides sufficient guidance such that the skilled worker could practice the claimed invention without performing an undue amount of experimentation.

The pending application was the first to teach a connection between vascularization and sonic hedgehog signaling. And, as discussed in several of Applicants’ previous Responses, it

was well understood by the skilled worker at the earliest effective filing date, as it is well understood by the skilled worker today, that inhibition of the blood supply feeding a tumor could be used as a treatment for cancer. The skilled worker also was aware of several means of preparing therapeutic antibody formulations, administering antibody treatments, determining appropriate antibody doses and analyzing antibody treatment efficacy in subjects suffering from breast cancer, a disease associated with excess vascularization and neovascularization. *See, e.g.,* Valone *et al.*, 1995, *Journal of Clinical Oncology*, 1995, 13(9): 2281-2292 (Exhibit A) and Weiner *et al.*, 1995, *Cancer Research*, 1995, 55:4586-93 (Exhibit B). The skilled worker, turning to the pending application and the teachings in the art, could have easily utilized the claimed method without undue experimentation. For these reasons, the application need not provide an *in vivo* working example in order to enable the pending claims.

B. Effectiveness of the Claimed Method

The Examiner's predominant ground for maintaining the outstanding enablement rejection appears to be based on the Examiner's belief that the claimed method allegedly would be ineffective in cases in which Shh signaling is not misregulated, and that the specification allegedly does not provide guidance as to a means of determining whether a solid tumor has misregulated Shh signaling. Accordingly, the Examiner concludes that the claims allegedly are not enabled by the application as filed. Applicants respectfully traverse.

As discussed in the landmark patent law case, *In re Wands*, a claimed invention need not be associated with complete success in order to be considered enabled by an application. *See, e.g., In re Wands*, 8 USPQ2d 1400, 1406 (Fed. Cir. 1988). Indeed, "partial success" may be considered sufficient for demonstrating enablement. *Id.* The skilled worker would have understood at the earliest effective filing date of the application, as the skilled worker still would understand today, that a given treatment or therapy for cancer would not be expected to cure each and every cancer patient. Rather, the skilled worker would have understood that a document teaching a treatment capable of inducing tumor regression in even a small percentage of a patient population would be enabling for the purpose of teaching an effective cancer treatment. For example, the pre-filing date document Sulkes *et al.*, 1994, *Br.J.Cancer*, 70: 380-83 (Exhibit C) teaches that docetaxel was capable of inducing partial remission in a relatively small subset of treated patients during Phase II clinical trials. Despite docetaxel's "partial

success” as a treatment for cancer, docetaxel was not dismissed as being an “unpredictable” or “ineffective” cancer therapy. Rather, docetaxel (Taxotere™) went on to become one of the most common treatments of numerous types of cancers and to generate billions of dollars a year in sales revenues.

Similar to docetaxel, the claimed invention does not lack enablement simply because it may not be applicable for inhibiting vascular growth in all types of tumors. Indeed, despite the fact that a correlation was shown over seven years ago between docetaxel resistance and reduced p27 expression in breast cancer cells (Brown et al., 2004, *Breast Cancer Research*, 6(5): R601-607- Exhibit D), Applicants could find no evidence that breast cancer patients are now screened for p27 expression before determining whether docetaxel administration is appropriate. The reason for this is that docetaxel administration is not typically used as a personalized cancer treatment, but rather as a cancer treatment generally. Such is the state of the art for cancer therapies and this state of the art applies equally to the claimed invention.

Similar to docetaxel, the claimed method is effective in treating a number of different tumor types (*See, e.g.*, Bailey et al., 2009, *Oncogene*, 28(40): 3513-25; Yauch et al., 2008, *Nature*, 455: 406-412; Coon, et al., 2010, *Mol Cancer Ther.*, 9(9): 2627-36; Berman, 2003, *Nature*, 425: 846-850- enclosed as Exhibits E-H). Considering the wide variety of different tumor types in which the claimed treatment has been shown to be effective, combined with the skilled worker’s expectation that a given cancer therapy would be ineffective in at least a subset of tumors, the skilled worker would not have been required to perform any undue experimentation in order to utilize the claimed method.

Considering the teachings in the application, the level of skill in the art, and the skilled worker’s understanding of what it meant to employ a “successful” treatment of tumors, the pending claims are enabled by the application as filed.

C. Enablement Rejection: Conclusion

For all of the reasons discussed above, the amended claims are enabled by the application as filed. Applicants respectfully request that the Examiner reconsider and withdraw the Enablement rejection.

Co-Pending Applications

Applicants take this opportunity to update the Examiner on the status of various co-pending applications. Applicants invite the Examiner to consider all prior, ongoing, and future prosecution in these co-pending applications. Application serial number 10/652,298 issued May 4, 2010 as U.S. Patent No. 7708998. Application serial number 10/652,686 issued March 3, 2009 as U.S. Patent No. 7498304. Application serial number 10/727,195 issued April 6, 2010 as U.S. Patent No. 7691593. The most recent action in application serial number 12/791,785 is an October 6, 2011 Response to a Final Office Action mailed on July 11, 2011. The most recent action in application serial number 12/728,948 is a November 1, 2011 Response to an August 1, 2011 communication. The most recent action in application serial number 12/756,939 is a non-final Office Action mailed on November 2, 2011.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our **Deposit Account No. 18-1945, under Order No. under Order No. HC-P02-060.**

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Respectfully submitted,

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